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ATTORNEY DOCKET NO. CONFIRMATION NO. FILING DATE FIRST NAMED INVENTOR APPLICATION NO. Chia-Lin Wei 00801.0197.NPUS00 1716 09/864,637 05/23/2001 EXAMINER 7590 02/18/2004 STRZELECKA, TERESA E John C. Robbins Large Scale Biology Corporation 3333 Vaca Valley Parkway Suite 1000 ART UNIT PAPER NUMBER Vacaville, CA 95688 1637

DATE MAILED: 02/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## **Advisory Action**

Application No.	Applicant(s)	
09/864,637	WEI ET AL.	
Examiner	Art Unit	
Teresa E Strzelecka	1637	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 26 January 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

Examination (RCE) in compliance with 37 CFR 1.114.	
PERIOD FOR REPLY [check either a) or b)]	
a) $\square$ The period for reply expires $\underline{5}$ months from the mailing date of the final rejection.	:
b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, we no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION 706.07(f).	ction.
Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the applied have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The applied under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rej timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).	propriate extension al Office action; or
1. A Notice of Appeal was filed on Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.	
2. The proposed amendment(s) will not be entered because:	
(a) ⊠ they raise new issues that would require further consideration and/or search (see NOTE below);	;
(b) ☐ they raise the issue of new matter (see Note below);	:
(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or s issues for appeal; and/or	implifying the
(d) they present additional claims without canceling a corresponding number of finally rejected claim	ns.
NOTE: the newly added claims 47-51 require further search.	:
3.⊠ Applicant's reply has overcome the following rejection(s): <u>See Continuation Sheet</u> .	
4. Newly proposed or amended claim(s) would be allowable if submitted in a separate, timely filed canceling the non-allowable claim(s).	d amendment
5. The a) affidavit, b) exhibit, or c) request for reconsideration has been considered but does NO application in condition for allowance because:	OT place the
6. The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which we raised by the Examiner in the final rejection.	re newly
7.⊠ For purposes of Appeal, the proposed amendment(s) a)⊠ will not be entered or b)☐ will be entered explanation of how the new or amended claims would be rejected is provided below or appended.	and an
The status of the claim(s) is (or will be) as follows:	
Claim(s) allowed:	-
Claim(s) objected to:	
Claim(s) rejected: <u>15-31 and 43-45</u> .	
Claim(s) withdrawn from consideration:	•
8. The drawing correction filed on is a) approved or b) disapproved by the Examiner.	÷
9. Note the attached Information Disclosure Statement(s)( PTO-1449) Paper No(s)	/ .
10. Other:	
JEFFREY FREI	DMAN MINER

Continuation of 3. Applicant's reply has overcome the following rejection(s): rejection of claims 1-8, 10-32 and 37-46 under 35 U.S.C. 112 second paragraph; rejection of claims 1-5, 7, 10-14 under 35 U.S.C. 103(a) over Nelson et al. and Frohman et al; rejection of claim 6 under 35 U.S.C. 103(a) over Nelson et al., Frohman et al. and Somerville et al.; rejection of claim 8 under 35 U.S.C. 103(a) over Nelson et al., rejection of claim 38 under 35 U.S.C. 103(a) over Nelson et al. and Gress et al.; rejection of claims 39-41 under 35 U.S.C. 103(a) over Nelson et al., Frohman et al. and Xu et al.; rejection of claims 32, 37 and 46 under 35 U.S.C. 103(a) over Nelson et al. and Carninci et al.

Applicants argue that claim 15 and the dependent claims are not obvious over the combination of Nelson et al. and Carninci et al., since (a) bothe Nelson et al. and Carninci et al. teach procedures of library normalization based on subtraction with drivers, and the goal of the claimed method is normalization not subtraction; (b) the drivers are not from a subgroup of high abundance clones of the library being normalized; (c) neither reference teaches separation of high abundance sample cDNAs into subgroups which are then hybridized to each other.

Regarding (a), both Nelson et al. and Carninci et al. teach library normalization. Regarding (b) and (c), Nelson et al. teach identification of members of the non-normalized library present in high amounts and in low amounts, i.e., generation of subgroups, by hybridization of the library with probes obtained from the same library (page 210, third and fourth paragraph; page 211, fourth and fifth paragraphs). Carninci et al. teach normalization of libraries by hybridization of full-length cDNAs to RNA from which the cDNAs were obtained and removing the abundant cDNA-RNA hybrids (Fig. 1; page 1625, last paragraph; page 1626, 1627; page 1628, paragraphs 1-6). In addition Carninci et al. teach preparation of minilibraries from the highly-abundant cDNAs, i.e., selecting subgroups of the highly-abundant members of the sample (page 1620, second and third paragraphs; page 1627, paragraphs 8 and 9; Table 1). The minilibraries are then used to identify more groups of highly abundant members (Table 1, see normalization of library 26-100). Therefore Nelson et al. and Carninci et al. teach all of the steps of the method of claim 15.